



# USDA and FDA Regulations: "The Attack of the Killer Tomato"

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USDA and FDA Regulations: The Attack of the Killer Tomato

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### Introduction

The mingling of science and food is not a new phenomenon. In fact, genetic improvement has played a major part in the development of our food supply for thousands of years. Wine, cheese, and yogurt, for example, were created through the use of microbes. Tangelos, white eggplants, and nectarines were products of selective breeding. In addition, American eating has long strayed from the predominant use of fresh, local, and natural foods. Food production has become big business, with economy and convenience ruling the food industry now that pesticides, preservatives, and processing have distanced food from the pure and agricultural and turned it into a ready-to-eat commodity available immediately on any supermarket shelf. Given its history of continually restructuring relationships with food, one would expect the public to accept any innovation, the government to be able to respond to any new regulatory challenge. Yet, today's crops have crossed a new line of agricultural creativity, and they have entered the realm of the unimaginable. Biotechnology has turned genetic improvement into genetic engineering; along with this new technology comes a barrage of new social and regulatory issues and concerns.

Genetically engineered foods have the potential to make great steps toward improving food and the environment. For example, biotechnology can be used to increase the food supply, as it can make each acre of land more productive through the use of fewer chemical sprays and the introduction of greater resistance to

plant diseases and pests.<sup>1</sup> By reducing the use of chemicals in agriculture, water contamination and the exposure to and disposal of pesticides could be curtailed. Scientific alteration is the future of the food industry— the USDA alone has around 1000 applications and notifications for field tests of genetically engineered produce, an indication of big changes ahead in what we eat and how it is grown— but are we ready for it?

Calgene, a California biotechnology company, has spent \$25 million on a genetically engineered fruit, the Flavr-Savr tomato, in order to have a quality tomato on the market year round. Instead of being forced to use green-picked tomatoes that are ripened for supermarkets using ethylene gas (the tomato's natural ripening agent), Calgene's product enables retailers to have a continuous supply of red, ripe tomatoes. To accomplish this, Calgene's researchers extracted the one gene in the tomato (out of its approximately 35,000) that controls softening during the ripening process. Then, they reversed the order of this gene's components, copied the result, and stuck it back into the fruit. This resulted in a slow ripening tomato that can stay longer on the vine to gain more flavor and that will keep its flavor over an extended shelf life (approximately 3 weeks).

Yet, what some view as a breakthrough others view as a curse. There has been a widespread backlash against genetic alteration of food. Consumer groups and advocacy organizations such as the Pure

<sup>1</sup>A *step* further than improving a plant's resistance to disease is the possibility of splicing genes that can be used as vaccines into plants, so that people who eat foods from these plants could potentially gain immunity to certain diseases. -, Industry, Government Pleased with Public's Acceptance of Biotech Plants, Food Chemical News, December 11, 1995, at 18.

Food Campaign have sprung up to resist the influx of genetically altered foods into the marketplace, and some chefs refuse to use such products in their kitchens.<sup>2</sup> In fact, Calgene has experienced continuous fiscal losses despite thorough regulatory approval of its product, as the Flavr-Savr has only attracted \$14 million of the \$4 billion that American consumers spend on tomatoes each year.<sup>3</sup> The predominant fear is that engineers will create exotic or monster plants that will have the ability to do things that could never occur in nature and that can have uncertain effects upon those who eat the products of such plants—or at the very least, that plants could become weed-like, resistant to disease and pesticides, and spread.

Those concerned about genetic alteration of food cite various reasons to support their position. First, the genetic engineering process is often considered different from traditional plant breeding. While conventional plant breeders regularly attempt to introduce desirable genes from wild varieties into promising commercial varieties of food crops, they usually do so by transferring large numbers of various genes, and the results are often fairly unpredictable. In contrast, genetic engineers transfer very few genes (in the case of the Flavr-Savr, only one gene), bringing changes that are very clearly defined and predictable. Just as people fear genetic selection in humans becoming a quest to create ideal offspring by choosing very

<sup>2</sup> This has even reached Cambridge, MA, as the menu at Christopher's restaurant

in Porter Square conspicuously states that the establishment does not use any genetically engineered foods!

~ Greg Beaubien, Battle Over Genetics, Chicago Sun-Times, Nov. 19, 1995, at

65.

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animal genes inserted into plants were extracted from non-kosher animals, such as pigs. In addition, many believe that it would be generally dangerous to the natural balance of the ecosystem to give plant species animal characteristics, or to apply gene technology to other parts of the food chain. ~

Finally, hesitancy toward genetically engineered crops is culturally based. People are opposed to the idea of mono-crops in agriculture and giving up the notion of season. We are used to not having all fruits and vegetables at their peaks 365 days a year, and as a society we have come to expect certain times of the year to yield the best flavors of different products. Tomatoes are supposed to be best in the summer, so it is strange to think of January as a time for fresh summer produce. After all, if we could control the weather, would we really want to have a perpetual spring and eliminate the winter completely?

This paper will address the U.S. response to the present and future use of the genetic alteration of food through the analysis of the pioneer food product— the Flavr-Savr tomato— which was the first genetically altered food to be approved for the United States market. As the first bioengineered produce to clear regulatory hurdles, the Flavr-Savr required governmental agencies to adapt their current standards to a new realm of food and agriculture and to consider how genetically altered foods fit into the United States regulatory scheme. By tracing the regulatory history of the Flavr-Savr and examining both agency and public

<sup>4</sup>For example, a recent article in ~ contemplated transferring human genes to cows so that they could produce 'human milk for babies. February 9, 1996, at 19.

specific genes for the unborn, people envision the gene selection process becoming so specific as to take all that is natural and diverse out of agricultural production.

In addition, there is hesitancy to accept the transfer of genes inter-species. Biotechnology can go a notch further than nature by mingling the genes of not just plants with other plants, but even of plants with insects, plants with bacteria, plants with viruses, and plants with animals. The Flavr-Savr is actually a relatively unique example in the world of genetically altered foods, because it involves the modification of only one gene, and that is a gene from the tomato itself (in addition to helper genes for antibiotic-resistance); thus, the Flavr-Savr could arguably have been developed eventually through traditional methods and is not necessarily as controversial as other products on the drawing board. For example, there is greater potential for adverse effects if genes are switched from common allergens (such as peanuts) into other plants instead of switched within one plant species, as allergens may transfer to the resulting foods. Gene transplants from animals into plant products (such as one now abandoned project to transplant a gene from a cold-resistant fish into a tomato to make it frost-resistant) are even more counterintuitive to nature, and could potentially result in plants with strangely un-plant-like characteristics. There are also ethical and religious reasons often cited to oppose the use of animal products in agriculture. For example, vegetarians would not necessarily eat foods derived from plants engineered with animal genes, and kosher individuals may not eat such foods if the

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response to genetically altered food products, one can also project the likely regulatory future of genetically altered foods.

I have already addressed the basic characteristics of the Flavr-Savr, its anticipated place within the food industry, and popular concerns with genetically altered food. The rest of this paper will be divided into three sections. Section I will trace the Flavr-Savr's path of USDA regulatory approval and the USDA's current procedure for approval; section II will similarly study the FDA's process of regulation. Finally, Section III will, in light of the procedures presently in place, consider the future of USDA and FDA regulations for genetically altered food products, and whether we can anticipate an eventual consolidation of regulatory schemes.

#### Section I: USDA Regulation and the Flavr-Savr Tomato

##### Statutory Authority

The USDA has broad statutory authority to regulate agricultural products. The Federal Plant Pest Act, which was enacted on May 23, 1957, gives the USDA authority to protect American agriculture against disease, injury, or damage by regulating the movement and existence of any plant pest when there is a danger of the dissemination of such a pest.<sup>5</sup> The USDA has interpreted its power to include authority over genetically altered plants, which can potentially be considered plant pests.

The Federal Plant Pest Act authorizes the USDA to:

~ 7 U.S.C.S. § 150 et. seq.

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promulgate such regulations requiring inspection of products and articles of any character whatsoever and means of conveyance, specified in the regulations, as a condition of their movement into or through the United States, or interstate, and imposing other conditions upon such movement, as [is deemed] necessary to prevent the dissemination into the United States, or interstate, of plant pests.<sup>6</sup>

The act defines plant pest as:

any living stage of any insects, mites, nematodes, slugs, snails, protozoa, or other invertebrate animals, bacteria, fungi, other parasitic plants or reproductive parts thereof, viruses, or any organisms similar to or allied with any of the foregoing, or any infectious substances, which can directly or indirectly injure or cause disease or damage in any plants or parts thereof, or any processed, manufactured, or other products of plants.<sup>7</sup>

The Federal Plant Pest Act also states that the USDA may refuse to issue a permit for the movement of any plant pest when.

- such movement would involve a danger of dissemination of such pests. <sup>8</sup> Furthermore, the USDA may enforce its decisions not only through civil and criminal penalties, but also through remedial measures:

Whereas, the existence of a plant pest new to or not theretofore known to be widely prevalent or distributed within and throughout the United States on any premises in the United States would constitute a threat to crops, other plant life, and plant products of the Nation and thereby seriously burden interstate or foreign commerce, whenever the Secretary determines that an extraordinary emergency exists because of the presence of such plant pest on any premises in the United States, and that the presence of such plant pest anywhere in the United States threatens the crops, other plant life, or plant products of the United States, the Secretary may. ... seize, quarantine, treat, apply other remedial measures to, destroy, or otherwise dispose of. ... any product or article of any character whatsoever.<sup>9</sup>

<sup>6</sup> ~ T.J.S.C.S. 5 l5Oee.

<sup>7</sup> ~ 7 I.J.S.C.S. 5 l5Oaa(c). Under 7 CFR 5 340.1, individuals are instructed to consult APHIS to determine whether an organism is a plant pest and thus subject to regulation. In addition, 7 CFR § 340.2 lists groups and taxa of organisms which are deemed to be or to contain plant pests.

<sup>8</sup> ~ U.5.C.S. 5 l5Obb(b).

<sup>9</sup> U.S.G.S. 5 l5Odd(b) (1)

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Finally, the Plant Quarantine Act,<sup>10</sup> originally enacted on August 20, 1912, gives supplementary authority to the USDA to regulate the importation and movement of nursery stock and other plants which may harbor injurious pests or diseases, and directs that such plants must be grown under certain USDA imposed conditions once in the United States.

7 CFR ~ 340: The Introduction of Organisms and Products Altered or Produced through Genetic Engineering

The USDA's regulatory authority over genetically altered foods is codified under 7 CFR § 340, which regulates the introduction of organisms and products altered or produced through genetic engineering which are plant pests or which there is reason to believe are plant pests. While 7 CFR § 340 was promulgated in June 1987, the USDA amended it in 1993, partially in response to its regulatory experience with the Flavr-Savr. Before promulgating the 1993 amendments, there were two major steps in the approval process for genetically altered agricultural products: a grant of a permit for introduction of the organism, and a grant of non-regulatory status. In the course of its path toward USDA approval, the Flavr-Savr followed both of these steps.

1. *Acquiring a Permit for Introduction*

At the time Calgene sought the introduction of the Flavr-Savr into the market, the first procedural step for a genetically altered product under 7 CFR § 340 was obtaining a permit for the

<sup>10</sup> ~ U.S.C.5. § 151 et. seq.

11 ~ CFR § 340.1.

127 CFR §340.4(b).

introduction of any regulated article through importation, interstate movement, or release into the environment. Regulated articles are, generally speaking, organisms that have been altered or produced through genetic engineering that are plant pests or that reasonably could meet the definition of plant pest. Regulated article is specifically defined in 7 CFR § 340 as follows:

any organism which has been altered or produced through genetic engineering, if the donor organism, recipient organism, or vector or vector agent belongs to any genera or taxa designated in §340.2 and meets the definition of a plant pest, or is an unclassified organism and/or an organism whose classification is unknown, or any product which contains such an organism, or any other organism or product altered or produced through genetic engineering which the Director, BEEP, determines is a plant pest or has reason to believe is a plant pest. Excluded are recipient microorganisms which are not plant pests and which have resulted from the addition of genetic material from a donor organism where the material is well-characterized and contains only non-coding regulatory regions. ~

The Flavr-Savr was considered a regulated article for purposes of introduction under 7 CFR § 340 because unlike products derived through natural selective breeding, plant pathogen sources were used in its development. Thus, Calgene had to apply for a permit to be able to conduct field testing with the Flavr-Savr— that is, to introduce the tomato into the environment through experimentation.

The procedure for acquiring such a permit for experimentation was quite lengthy. Application had to be made at least 120 days in advance of the proposed release. 12 In addition, there were extensive informational disclosure requirements, encompassing

general identification and several detailed reports, including the following:

- a description of the anticipated or actual expression of the altered genetic material in the regulated article and how that expression differs from the expression in the non-modified parental organism (e.g. morphological or structural characteristics, physiological activities and processes, number of copies of inserted genetic material and the physical state of this material inside the recipient organism (integrated or extrachromosomal), products and secretions, growth characteristics <sup>13</sup>

- a detailed description of the molecular biology of the system. .. which is or will be used to produce the regulated article<sup>14</sup>

- a detailed description of the purpose for the introduction

- of the regulated article including a detailed description of the proposed experimental and/or production design<sup>15</sup>

- a detailed description of the processes, procedures, and safeguards which have been used or will be used in the country of origin and in the United States to prevent contamination, release, and dissemination in the production [of the regulated article]<sup>16</sup>

- a detailed description of the intended destination. uses and/or distribution of the regulated article (e.g. greenhouses, laboratory, or growth chamber location; field trial location; pilot project location; production, propagation, and manufacture location; proposed sale and distributional location)<sup>17</sup>

- a detailed description of the proposed procedures, processes, and safeguards which will be used to prevent escape and dissemination of the regulated article at each of the intended destinations<sup>18</sup>

As is evident by the extensive procedure outlined above, the USDA made it relatively difficult for any genetically altered article to gain permission for introduction through movement and

13 ~ CFR § 340.4(b) (5).

14 ~ CFR § 340.4(b) (6).

15 ~ CFR § 340.4(b) (8).

16 ~ CFR § 340.4(b) (10).

17 ~ CFR § 340.4(b) (11).

18 ~ CFR § 340.4(b) (12).

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experimentation, let alone for deregulation and marketing. Yet, Calgene successfully obtained a permit for introduction to conduct field testing. It then proceeded to a previously untested step in the USDA regulatory process for genetically altered plant products— to attempt to switch from regulated to non-regulated status.

2. *Obtaining Non-Regulatory Status*

On July 14, 1992, the Animal and Plant Health Inspection Service (APHIS) published a notice in the Federal Register stating that Calgene had filed a petition for the Flavr-Savr to assume non-regulated status and requesting comments on a proposed interpretive ruling concerning this petition.<sup>19</sup> Calgene had requested that the Flavr-Savr tomato's status as a regulated article under 7 CFR § 340 be changed, alleging that it did not present a plant pest risk under the Federal Plant Pest Act. A decision to deregulate would mean that the Flavr-Savr tomato would no longer need permits from APHIS for release into the environment, importation, or interstate movement, and that any cultivation, propagation, movement, and crossbreeding with other non-regulated tomato lines could be conducted freely.

On October 19, 1992 (after a comment period of 45 days which had ended on August 28, 1992), APHIS announced its issuance of the interpretive ruling on Calgene's petition.<sup>20</sup> Based upon written comments submitted to the USDA, a review of scientific literature, expert opinion from tomato breeders and pathologists, data

<sup>19</sup> 57 Fed. Reg. 31170 (July 14, 1992)

<sup>20</sup> ~ Fed. Reg. 47608 (Oct. 19, 1992)

submitted by Calgene, and the biological and observable properties of the tomato itself,<sup>21</sup> APHIS agreed that the Flavr-Savr would no longer be considered a regulated article. The scope of the interpretive ruling applied only to the Flavr-Savr tomato, and only to those Flavr-Savr tomato lines that had already been field tested under the auspices of the USDA, so that new tomato lines carrying different marker genes were not included.<sup>22</sup>

A USDA decision that an organism does not present a plant pest risk signifies that there is reasonable certainty that the organism cannot directly or indirectly cause disease, injury, or damage when grown, stored, sold, or processed. This kind of decision requires evaluating the existence of pathogens, weediness, and harmful effects on beneficial organisms. In its interpretive ruling, APHIS came to five basic conclusions that would later help set the regulatory standard of future USDA evaluations for the potential deregulation of genetically altered agricultural products. These conclusions express the agency's general belief that there is no reason to fear the possibility of certain genetically altered plants overrunning or damaging other plants:

1- The Flavr-Savr exhibits no Plant Pathogenic properties.

First, since the plasmids used in the construction of the Flavr-Savr are disarmed, they cannot replicate

21 ~ was only after the deregulation of the Flavr-Savr that the USDA

finalized the process for assuming non-regulated status. This process is addressed in the 1993 amendments to 7 CFR § 340, which are discussed below. 22 Since the Flavr-Savr's regulatory approval, Calgene has submitted and been cleared for the non-regulation of numerous tomato lines in addition to those few which were deregulated in 1992. ~ 59 Fed. Reg. 50220 (October 3, 1994), 59 Fed. Reg. 59746 (November 18, 1994), 60 Fed. Reg. 15284 (March 23, 1995), and 60 Fed. Reg. 38788 (July 28, 1995)

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themselves. In addition, the transferred genetic material in the Flavr-Savr is considered stable; that is, it will not persist in the environment outside of the direct cultivation process. Third, neither the transferred gene nor the antibiotic resistance marker gene (the kanamycin resistance gene) in the Flavr-Savr is likely to cause disease or damage to any other plant.

2- The Flavr-Savr is no more likely to become a weed than non-engineered Darental varieties  
. In

general, the tomato is a highly domesticated plant that does not persist without human intervention; the FlavrSavr is so similar to the traditional tomato that it, too, has little potential to become a successful weed.

3- The Flavr-Savr is unlikely to increase the weediness Dotential of any other cultivated or wi  
. The tomato does not

cross-pollinate with other plants in the United States without human intervention, and commercial tomatoes are virtually self-pollinating, so it is not likely that the tomato will increase the weedy potential of other plants.

4- The Flavr-Savr does not cause damaae to Drocesses<sup>1</sup> agricultural commodities.  
Processing the Flavr-Savr

tomato plant should not create increased susceptibility toward disease or damage.

5- The Flavr-Savr is unlikely to harm other organisms that are beneficial to agriculture  
. Since no toxic components

or pathogenic properties were located in the Flavr-Savr, there is no reason to believe that any organisms (such as bees) could be adversely affected by its existence.

*The 1993 Amendments to 7 CFR ~ 340*

Partially in response to its regulatory experience with the Flavr-Savr tomato, APHIS set forth a proposed rule to amend 7 CFR § 340 in November 1992.<sup>23</sup> On March 31, 1993 APHIS published a final rule regarding this matter;<sup>24</sup> this rule became effective on April 30, 1993. The amendments to 7 CFR § 340 altered USDA regulation of genetically altered products in two basic ways. First, the USDA instituted a more lenient notification process under §340.3 for the introduction of six previously regulated types of plants. Thus, the notification process provided an easier regulatory alternative for corn, tomato, cotton, tobacco, soybean, and potato while the traditional, lengthy petition process for introduction of organisms remained in place for all other crops. Second, based upon the deregulation of the FlavrSavr, the USDA set out a new petition procedure for determinations that certain genetically altered agricultural products would be deregulated.

*7 CFR ~340.3: Notification for the Introduction of Certain Regulated Articles*

23 57 Fed. Reg. 53036 (November 6, 1992).

24 58 Fed. Reg. 17044 (March 31, 1993).

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The decision to allow six major crops (potato, corn, soybean, tomato, cotton, and tobacco) to be subject only to a notification process instead of to a mandatory full-blown permit evaluation was based on the USDA's collective experience (from 1987 to 1993) with genetically altered plants. Within that time, the USDA granted 365 permits for importation and release into the environment and

1301 permits for interstate movement for organisms which had been developed with genetic material from plant pests. Of these permits, 85% were granted for the six types of plants designated in 7 CFR § 340 as subject to the new notification process. <sup>25</sup>

The USDA's extensive regulatory evaluations of tomato, corn, soybean, potato, cotton, and tobacco prior to allowing their introduction into the environment through experimentation and field testing had confirmed that the genetically altered versions of these crops presented largely the same ecological concerns (e.g. weediness, competitiveness, toxicity) as their traditional counterparts. The USDA's evaluation of the Flavr-Savr was cited as support for the new lenient notification process for experimentation. Determining that the Flavr-Savr should have non-regulated status provided the USDA with the experience of assessing the potential for gene transfer from genetically altered, commercially popular plants such as the tomato; as a result, the agency found any such potential to be negligible. While APHIS expressed receptivity to adding other species to the six-crop list in the future, it confined its initial list to these

<sup>25</sup> ~ 58 Fed. Reg. 17044 (March 31, 1993) . Specifically, the percentages of total permits were issued as follows: corn (19%), cotton (10%), potato (20%), soybean (18%), tobacco (5%), and tomato (13%)

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six crops because they had been the most actively field tested and thoroughly considered. The lenient notification process under 7 CFR § 340 only provides for private experimentation; because the USDA regulates field testing and requires that tests only exist under confined, controlled conditions, it seemed logical that such carefully monitored cultivation would not present increased risk to the environment and other organisms.<sup>26</sup> APHIS also expressed its belief, though, that experimentation and interstate movement of genetically altered versions of the six crops would not pose any additional risk to the dissemination of plant pests.

In order to be eligible for the new notification procedure, genetically altered agricultural products must meet the following criteria:

1. The article must be one of the six species mentioned above. The USDA acknowledged that it would be amenable to adding new plant species to the six species mentioned above when such additions are deemed appropriate in the future.<sup>27</sup>

<sup>26</sup> ~ would like to note that while the USDA does not have special National Environmental Policy Act (NEPA) requirements, it must comply with NEPA's standard provisions requiring the preparation of environmental evaluations when major federal action 'significantly affects the quality of the human environment. APHIS had prepared individual environmental assessments and findings of no significant impact (FONSI's) for all permit evaluations between 1987 and 1993. As these inquiries led the USDA to decide that the six crops now qualifying for the new notification scheme presented no significant environmental impact, the USDA anticipated eliminating a need for NEPA environmental evaluations for these crops on a case-by-case basis in the future. Testing organisms other than those of the six notification crops are still regulated under traditional permit procedures, and thus must still comply with the preparation of case-by-case environmental assessments and environmental impact statements whenever necessary under the requirements of NEPA.

<sup>27</sup>Interestingly, the USDA's proposed rule for amending 7 CFR § 340 (57 Fed. Reg. 53036, Nov. 6, 1992) had contemplated the possibility of decentralizing the decision to add other species to the list by providing for eligibility decisions at the level of an appropriate Institutional Biosafety Committee.

2. The introduced genetic material is stably integrated— that is, that it cannot replicate itself.
3. The function of the genetic material is known, and does not cause plant disease.
4. The introduced genetic material does not cause the production of infectious entities, encode substances that are likely to be toxic to other organisms, or encode products intended for pharmaceutical use. These are all serious consequences that should not be ignored with a lenient notification process.
5. The genetic sequences used must not pose a significant risk of the creation of any new plant virus.
6. The plant cannot contain certain genetic material derived from human or animal pathogens. 28

Furthermore, the notification process under 7 CFR § 340.3 incorporates performance standards. These standards, which are similar to those required for the traditional permit process,

The USDA removed this provision from the final rule in response to comments that such a committee (and various state authorities, for that matter), lacked the expertise to make such determinations that such a provision would amount to self-regulation by researchers, and that the proposed committee would have no public accountability for its actions. The authority to add new species to the six crops mentioned in the final rule, then, now remains with APHIS for public accountability, consistency, and liability purposes. See, 59 Fed. Reg. 17044. (March 31, 1993).

<sup>28</sup>APHIS specifically noted that it was not purporting to infringe upon existing federal authority (i.e. FDA, EPA) through the regulation of pathogens, but that this requirement was necessary to enable the USDA to oversee the introduction of plants containing any genetic material that has never been expressed in plants before.

provide additional guarantees against adverse effects on the environment due to gene transfer from the six plant species to other plants. For example, regulated articles must be adequately contained so they will not be released into the environment, and they must not be mixed inadvertently with non-regulated plants that are not part of the approved environmental release. In addition, all field trials must be conducted so that the regulated article will not persist in the environment without human intervention.

Procedurally, the notification process for the six specified crops is much less rigorous than the traditional permit process. The USDA requires only basic identification and general information about the imminent introduction of the plant, including the source of the genetic material, the method by which the recipient organism was transformed, the size and location of the introduction, and a statement certifying that introducing the regulated article will be in accordance with the provisions of the applicable sections of the 7 CFR § 340.29. Notifying the USDA only has to be accomplished thirty days prior to the importation or environmental release of the product (in comparison with the 120 day requirement of the traditional permit process), and ten days prior to the day of an interstate movement.<sup>30</sup> Finally, field test reports must be submitted to the USDA every year during the occurrence of the field tests, and any unusual occurrences must be reported immediately. These data reports were perceived by the

297 CFR § 340.3(d).

<sup>30</sup>In fact, the proposed USDA rule suggested ~ notification as introduction, but concern about public perception and the need for review on the state level prompted the agency to change its mind!

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USDA as not only being crucial to safety, but also as essential for step two in the USDA's regulatory regime—evaluations to determine the potential for switching a product from regulated to non-regulated status.

*7 CFR p340.6: Petition for the Determination of Nonregulated Status*

Because the USDA projected imminent growth in the development of genetically altered plants, clarifying the petition process for all determinations that regulated plants should assume non-regulated status was a natural choice for the second major 1993 amendment to 7 CFR § 340. The USDA chose to formalize a procedure similar to that which it had used for the first genetically altered crops considered by the agency; it basically codified the same evaluation process which the Flavr-Savr went through. In fact, the issues which the USDA decided to consider with regard to all decisions for nonregulatory status under 7 CFR § 340.6 (c) (4) were derived from the five conclusions which were articulated in the Flavr-Savr's interpretive ruling for non-regulated status. According to 7 CFR 340.6(c) (4), this includes (but is not limited to)

plant pest risk characteristics, disease and pest susceptibilities, expression of the gene product, new enzymes or changes to the plant metabolism, weediness of the regulated article, impact on the weediness of any other plant with which it can interbreed, agricultural or cultivation practices, effects of the regulated article on nontarget organisms, indirect plant pest effects on other agricultural products, transfer of genetic information to organisms with which it cannot interbreed, and any other information which the Director believes to be relevant to a determination. Any information known to the petitioner that indicates that a regulated article may pose a greater plant pest

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risk than the unmodified recipient organism shall also be included.

Furthermore, APHIS requires all available experimental data, scientific literature and publications, unpublished studies, and a description of the differences in genotype between the regulated article and the nonmodified recipient organism. 31 Finally, APHIS extended the 45 day public comment period to 80 days, and the 120 day review period to 180 days in order to accommodate public concern and to provide an opportunity for response from the public, the industry, and the scientific community. Based upon the existence of such extensive informational requirements, it is evident that the process for attaining non-regulated status was meant to be quite comprehensive. Perhaps close scrutiny was deemed important at the final stage of regulatory checks in order to compensate for leniency in granting permits for experimentation and field testing through notification. The Flavr-Savr went through fairly rigorous analysis; similarly, the USDA seemed to anticipate a thorough evaluation of all genetically altered products. The major step taken in the 1993 amendments was, however, that for six crops, thorough evaluation would no longer be required at every regulatory step—such scrutiny was reserved instead for the deregulation stage.

#### Section II: The FDA and the Flavr-Savr Tomato

##### *Stationary Authority*

The Food and Drug Administration is the primary federal agency responsible for ensuring the safety of commercial food and

31 ~ CFR § 340.6(c)

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food additives. Under the Federal Food, Drug, and Cosmetic Act, the FDA has broad authority to ensure the safety and wholesomeness of food. Under section 402(a) (1) of that act, a food is deemed adulterated and unlawful if:

it bears or contains any poisonous or deleterious substance which may render it injurious to health; but in case the substance is not an added substance such food shall not be considered adulterated under this clause if the quantity of such substance in such food does not ordinarily render it injurious to health.

If producers of food are careful to ensure that food is safe, FDA enforcement mechanisms under this provision do not come into play, as the agency relies primarily on postmarket review and not on premarket evaluations of food products.

In contrast, however, under section 409(a) of the Federal Food, Drug, and Cosmetic Act, food additives are deemed to be unsafe unless premarket approval is given by the FDA. Congress provided for a premarket approval requirement in evaluating additives, with a science-based safety standard by which one must demonstrate to a reasonable certainty that no harm will result from the intended use of the additive. Once this standard is met, FDA regulations specify the conditions under which the additive may be safely used. The food additive rules do provide an exception to mandatory premarket review, however, as if substances are generally recognized as safe (GRAS) they are excluded from the definition of food additives, and are thus not subject to premarket review. A substance is considered GRAS if its safety has been recognized through a long history of use in food or if information available regarding the substance shows no danger of a

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safety concern necessitating premarket review. The FDA recommends consulting with the FDA to determine whether a substance is GRAS.

Producers of new foods are obligated to independently ensure that the foods they enter into the marketplace are safe. Since the FDA is empowered under the Federal Food, Drug, and Cosmetic Act to initiate ex post legal action through seizure, injunction, and criminal prosecution against any food found to be adulterated or misbranded within the meaning of the Act, however, food manufacturers often consult with the FDA concerning potential safety and regulatory issues. This is especially true with regard to new food products which are produced using innovative methods and new technology (such as the use of biotechnology for creating genetically engineered foods). Although such consultations are optional, the FDA encourages them in order to reduce the danger of potentially adverse impacts on human and animal food safety. Calgene actively sought FDA evaluation of the Flavr-Savr tomato as a protective measure before introducing its product into the market.

*The Flavr-Savr and the FDA*

Calgene's requests that the FDA evaluate the Flavr-Savr tomato marked the first involvement the FDA had with foods produced through the use of new methods of gene transfer. Calgene first contacted the FDA regarding the Flavr-Savr by filing two petitions. In the first petition, Calgene asked for an advisory opinion concerning whether the Flavr-Savr would be classified as



food and treated the same as traditional tomato varieties. <sup>32</sup> In the second petition, Calgene requested an advisory opinion regarding whether the kanamycin resistance gene, the selectable marker gene used in the production of several genetically altered foods including the Flavr-Savr, could be evaluated by the FDA for use. ~ After the FDA released a policy statement on foods derived from new plant varieties in 1992 (discussed below), Calgene resubmitted its petition regarding the kanamycin resistance gene in light of its potential to be considered a food additive. It revised its previous request and asked instead that the food additive regulations be amended to provide for the safe use of the kanamycin resistance gene as a processing aid. ~

In May 1994, the FDA published responses to both of Calgene's requests. First, the FDA concluded that the Flavr-Savr has not been significantly altered when compared to varieties of tomatoes with a history of safe use, and that it could therefore be considered food and treated the same as traditional tomato varieties.<sup>35</sup> This decision was made after the FDA evaluated the Flavr-Savr in light of the factors indicated in the FDA's policy statement of 1992. Second, the FDA decided to amend the food additive regulations to provide for the safe use of the kanamycin resistance gene as a processing aid for developing new varieties

<sup>32</sup> 57 Fed. Reg. 22772 (May 29, 1992)

See 56 Fed. Reg. 20004 (May 1, 1991). The kanamycin resistance gene is used to mark the specific genes that determine desired traits, thus aiding in the development of genetically altered foods with narrowly defined genetic changes. Since the marker gene persists in low levels in foods derived from the genetically altered plants (it would add very small amounts of a new protein to the diets of the consumers of the product), Calgene brought the substance to the attention of the FDA.

<sup>58</sup> Fed. Reg. 38429 (July 16, 1993)

<sup>59</sup> Fed. Reg. 26647 (May 23, 1994)

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of tomato, oilseed rape, and cotton. <sup>36</sup> This decision was based upon reviewing data submitted by Calgene and upon the results of a meeting of the FDA'S Food Advisory Committee in April 1994 (along with outside consultants representing various scientific disciplines). This meeting addressed the kanamycin resistance gene in particular and the FDA approach to evaluating the safety of foods in general, using the Flayr-Sayr tomato as an example as the focus of the meeting.

The FDA came to several conclusions regarding the kanamycin resistance gene. With regard to its safety for digestion, Calgene proved that the enzyme is inactivated by stomach acid and degraded by digestive enzymes, that it is not toxic, and that its estimated dietary exposure would be extremely low. In addition, the FDA determined that exposing processed food products to high temperatures would denature any enzymes which could have an adverse impact on the therapeutic effectiveness of antibiotics. Also, in unprocessed, fresh foods the enzyme would be degraded enough through digestion to prevent any problems. The FDA stated that other selectable marker genes (for uses similar to that which the kanamycin resistance gene serves) would be evaluated on a case by case basis.

Through its evaluation of the Flayr-Sayr, the FDA was able to glean enough experience to develop a workable regulatory system by which the food products of genetically altered plants could be analyzed and approved for sale in the market. The FDA's attention

<sup>36</sup> 59 Fed. Reg. 26700 (May 23, 1994) . Specifically, the FDA approved the use of the protein APh(3 minutes) II that is synthesized upon direction of the kanamycin resistance gene.

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to the Flavr-Savr and the Flavr-Savr's role in setting a market precedent helped enable the agency to publish a policy statement addressing the future regulation of genetically altered foods. Had the policy statement not been published, it seemed likely that other genetically altered foods would follow the path of the Flavr-Savr and seek out comprehensive analysis and approval. Instead, the FDA articulated a position that foods derived from new plant varieties would not have to pass through the extensive regulatory hurdles through which the Flavr-Savr traveled.

*FDA Policy Statement of 1992*

Because the FDA had received inquiries from industry, government agencies, academia, and the public requesting an authoritative articulation of the regulatory status of genetically altered foods, the FDA published a policy statement on foods derived from new plant varieties in May 1992. ~ This policy statement interprets the Federal Food, Drug, and Cosmetic Act with respect to the use of biotechnology in the production of food, and was an attempt to resolve regulatory issues prior to the widespread introduction of genetically altered foods into the marketplace. It addresses the potential need for premarket review, agency jurisdiction, informational requirements, and labeling; thus, the policy statement is an invaluable tool in analyzing the FDA's positions with respect to genetically altered foods. The views taken by the FDA with regard to genetically altered foods had contributed to the agency's decision to support

57 Fed. Reg. 22984 (May 29, 1992)

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the entry of the Flavr-Savr into the marketplace.<sup>38</sup> An overview of the most significant aspects of the policy statement follow.

The 1992 policy statement emphasizes that FDA regulation of food is mainly concerned with the objective characteristics and the intended use of food products, and not necessarily with the method by which a food is developed (though studying methodology may sometimes contribute to a complete understanding of the characteristics of a food product). Thus, merely because a food is genetically altered is not automatic cause for regulatory worry; the FDA is generally concerned with the nature of finished foods. Consequently, the policy statement essentially stands for the proposition that traditional regulatory procedures under the Federal Food, Drug, and Cosmetic Act should remain the primary legal mechanisms to ensure the safety of foods derived from genetically modifying processes. The FDA deemed its existing statutory authority and regulatory scheme to be adequate to ensure the safety of foods derived from new plant varieties, noting:

The existing tools. . . impose a clear legal duty on producers to assure the safety of foods they offer to consumers; this legal duty is backed up by strong enforcement powers, and FDA has authority to require premarket review and approval in cases where such review is required to protect public health.

This interpretation is fairly lenient towards genetically altered foods, which, according to the policy statement, are held to the

38 Because calgene made its evaluation requests prior to the finalization of the policy statement, it was forced to use lengthy, standard requests for advisory opinions under 21 CFR 10.85 (notice and comment regulatory procedures) instead of using the recommendations set forth in the policy statement. In the 1992 statement, the FDA instructed all future requests for FDA consultation to be made consistent with the streamlined procedures and principles articulated in the policy statement. It is likely, however, that the FDA's determinations in the policy statement impacted its ultimate evaluation of the Flavr-Savr. 3957 Fed. Reg. 22984 (May 29, 1992), p. 163.

same general standards as traditional foods, and thus are not considered to be more dangerous or to require unusually stringent evaluation.

Traditional FDA regulation is primarily found under section 402(a) (1) of the Federal Food, Drug, and Cosmetic Act regulating the sale of foods that contain unacceptable levels of unintended and unexpected contaminants (including naturally occurring toxicants), and section 409 of the Federal Food, Drug, and Cosmetic Act, providing for the premarket review of all food additives not recognized as GRAS. While the FDA emphasized its continued authority to exercise premarket review and to use its enforcement powers under these two main food safety provisions, the agency doubted that foods derived from genetically engineered plants would present safety concerns. First, the FDA rejected the need for regulating genetically altered foods under section 402(a) (1) of the Federal Food, Drug, and Cosmetic Act. While the FDA set forth a set of considerations which producers should use before introducing foods derived from new plant varieties into the marketplace (described below), ultimate decisions to market genetically altered food products are left to the producers, subject to FDA postmarket enforcement powers. Postmarket accountability was considered to be sufficient incentive for producers to maintain the high safety standards which characterize the U.S. food supply.

Second, the FDA evaluated the application of section 409 of the Federal Food, Drug, and Cosmetic Act. Since most food additives can only be used after premarket authorization, one

could theoretically see this requirement as a vehicle through which all genetically altered foods deemed to contain food additives could be forced through close scrutiny by the FDA. Section 201 of the Federal Food, Drug, and Cosmetic Act defines food additive as:

any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food. ... if such substance is not generally recognized among experts. ... as having been adequately shown through scientific procedures. ... to be safe under the conditions of its intended use.

In the policy statement, the FDA left open the Dossibility that transferred genetic material and the intended expression products (thus excluding unexpected or naturally occurring toxins) could potentially be subject to premarket review as food additives. However, the agency expressed doubt that added genetic material could present major food additive concerns, as the nucleic acids that are the major tools in genetic alteration of food are already universally present in living things— including every plant and animal used for food by humans or animals. Thus, such substances would most likely be considered GRAS, not likely to raise safety concerns, and not subject to premarket approval. The policy statement states:

When the substance present in the food is one that is already present at generally comparable or greater levels in currently consumed foods, there is unlikely to be a safety question sufficient to call into question the presumed GRAS status of such naturally occurring substances and thus warrant formal premarket review and approval by FDA. Likewise, minor variations in molecular structure that do not affect safety would not ordinarily affect the GRAS status of the substances and, thus,

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would not ordinarily require regulation of the substance as a food additive  
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The FDA, then, anticipated food additive concern as only likely to arise when new substances are injected into plants and consequently manifest themselves in the resulting food products.

Since phenotypic effects of any new trait are not always immediately and completely predictable, however, the FDA advised some level of consultation with the agency in order to assure that food products derived from new plant varieties would be analyzed for potentially adverse characteristics.. This is especially important when one considers that genetic alteration techniques such as the recombinant DNA technique used to create the FlavrSavr tomato have the ability to affect both what the FDA calls the agronomic traits (affecting such elements as disease resistance, insects and herbicides, and the ability to exist under certain environmental conditions) and quality traits (affecting such elements as processing, preservation, nutrition, and flavor of plants).

Though the FDA expressed a belief that the likelihood of safety hazards arising from genetic modification techniques would be very slim, the policy statement articulated the following eight potential effects which may require agency evaluation in order to assure food safety:

1. Unexpected effects. Unanticipated mutations can have an adverse effect on food products. However, the FDA expressed confidence that plant breeders using

40 57 Fed. Reg. 22984 (May 29, 1992)

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established scientific practices have successfully identified and eliminated plants that exhibit unexpected, adverse traits prior to commercial use.

2.       Known Toxicants. Many foods contain naturally occurring toxins that have the potential to be dangerous when they occur at high levels. The FDA expressed concern over the possibility that new plants can produce foods with high toxin levels. However, the FDA stated that plants with a long history of use that have not been associated with unusual toxicant characteristics are unlikely to present problems, because if toxicants do not present difficulties in parent plants, it is improbable that they will arise in genetically modified versions.

3.       NutrientS. The level of nutrients may be altered through genetic modification, affecting the potential nutrition of resulting foods.

4.       New Substances. Genetic engineers can introduce any substance into plants– even substances that would never occur naturally– and such substances should be evaluated for safety.

5.       ~ If genes are extracted from common food allergens and transferred into non-allergenic plants, this may result in foods with allergenic properties. Thus, labeling foods containing known or suspected allergens may be necessary.

6.       Antibiotic Resistance Selectable Markers. Selectable marker genes are used to isolate particular genes for

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particular traits, and persist in the eventual food products derived from genetically altered plants. The theoretical possibility exists that some of these marker genes could inactivate commonly used antibiotics when used for therapeutic reasons by humans.<sup>41</sup>

7. Plants Developed to Make Nonfood Substances, such as Polymers and Pharmaceuticals. The FDA wants to insure that non-food uses are not mixed or cross-bred with food uses. Nonfood chemicals that find their way into food products are considered a potential source of adulteration.

8. Animal Feed Issues. Since animals consume parts of plants that humans do not, and since the composition of animal diets is not as diverse as those of humans, any alteration in animal feed composition can be significant.

Because of the above eight concerns, the FDA articulated several considerations for the biotechnology industry to keep in mind as new food products are developed and compared with their traditional counterparts: 42

1. Characteristic toxicants of the host and donor species
2. The potential for allergen transfer

41 Note, however, that calgenes selectable marker, the kanamycin resistance gene, was approved for use pursuant FDA evaluation, and the food additive regulations were amended to provide for such use in 1994 (59 Fed. Reg. 26700, May 23, 1994). This issue is discussed in the next section, below.

42 The policy statement also contains a complex flow chart to be used by industry in evaluating and testing their products. 57 Fed. Reg. 22984 (May 29, 1992)

3. The concentration of nutrients
4. The safety and nutritional value of added proteins
5. The identity, composition, and nutritional value of carbohydrates, fats, and oils.
6. The effects of processing
7. The characteristics of the host plant and the donor plant
8. Metabolic considerations
9. Stability of the new plant variety. Food safety cannot be assured if genetic material is expressed at different levels in different generations.

The other issue addressed by the FDA in the policy statement was labeling. ~ According to section 403(i) of the Federal Food, Drug, and Cosmetic Act, food products must be described by its common or usual name (or an appropriately descriptive term), and reveal all material facts in light of representations suggested by labels. The FDA stated that foods derived from new plant varieties must be labeled only if they differ from [their] traditional counterparts such that the common or usual name no longer applies to the new food, or if a safety or usage issue exists to which consumers must be alerted. ~ The agency did not

43 I should also note that the FDA considered the applicability of NEPA to the regulation and use of foods derived from new plant varieties. Because the FDA anticipated that other agencies (for example, the USDA) may prepare environmental documentation, it expressed a desire to tier its environmental statements with those of other agencies in order to eliminate redundancy and repetition of similar issues. It intended to consult with APHIS whenever APHIS receives a petition for determination of regulatory status. However, the FDA does not consider safety consultations and regulatory advice regarding new foods to be agency action within the realm of NEPA requirements.

~ 57 Fed. Reg. 22984 (May 29, 1992) . The FDA cited the example of a tomato having a peanut protein, as such protein may cause an allergic reaction and should thus be included on the tomato's label.

determine, however, whether labeling should be required to distinguish all foods that were developed using genetic engineering techniques, as it was yet unclear whether the methods to develop such new plant varieties should be considered material and thus necessary information for labels. (The issue of labeling will be further addressed in Section III).

The policy statement, by articulating potential concerns that may arise in genetically altered foods, provided a solid framework by which foods derived from new plant varieties could move through FDA regulatory channels. The Flavr-Savr spurred the agency to set forth its positions, as it paved the way for other foods to seek entry into the market. The FDA seemed to back away from any commitments of thorough agency evaluation; however, it provided guidelines by which producers of novel foods could address major agency concerns.

### Section III: Analysis of Present and Future Regulation

#### Frameworks for Analysis

In June 1986, the Office of Science and Technology Policy published a Coordinated Framework for the Regulation of Biotechnology. <sup>51</sup> It designated the general scope of the various governmental regulatory agencies in the realm of biotechnology research. The Coordinated Framework states:

the agencies will seek to operate their programs in an integrated and coordinated fashion and together should cover the full range of plants, animals, and microorganisms derived by the

51 Fed. Reg. 23302 (June 26, 1986)

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new genetic engineering techniques. To the extent possible, responsibility for a product use will lie with a single agency 46

While the Coordinated Framework anticipated that genetically engineered products could be reviewed by the FDA for food uses, by the USDA for plant pests and animal pathogens, and by the EPA for pesticides according to each agency's traditional approval regimens, it also foresaw the possibility for overlapping jurisdiction, and left open the potential for the regulatory framework to evolve in light of experience.

In February 1992, the Office of Science and Technology published another guide for regulatory agencies. ~ It outlined a risk-based approach to be used by agencies in their evaluations of genetically altered products. Essentially, this document states that extensive evaluation should not be undertaken unless information concerning the risk posed by the introduction indicates that oversight is necessary. It recommends focusing on the characteristics and risks posed by finished products instead of concentrating on the process by which such products are created. This approach is based on the assumption that genetically modified products will not substantially differ from traditional products, so that stringent evaluation is not necessarily imperative. This risk based approach would seem to provide for eliminating unreasonable risk while keeping regulatory costs down and avoiding unnecessary evaluations.

46 51 Fed. Reg. 23302 (June 26, 1986).

57 Fed. Reg. 6753 (Feb. 27, 1992)

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These two frameworks for agency action raise interesting issues regarding the past, present, and future regulatory schemes subscribed to by the USDA and the FDA. For example, do the current USDA and FDA processes fit the general recommendations of the Office of Science and Technology? Are the agencies doing a good job of eliminating redundancy? What are the prospects for the future of the regulations for genetically altered products? Section III will address these and other issues raised in the regulation of the Flavr-Savr and other genetically altered plants and foods.

*A Trend Toward Relaxing Regulatory Responsibility*

It is apparent that the regulation of genetically altered food products bridges the jurisdictions of the USDA and the FDA. The USDA primarily concerns itself with the agricultural aspect of biotechnology, the FDA with the finished food; however, since every food product is inextricably linked to the plant that bears it, each agency has similar basic concerns and can evaluate very similar data to come to its respective regulatory decisions. For example, both agencies are concerned with the unanticipated effects of genetically altered products, the existence of toxins, and the existence of nonfood substances in newly genetically altered plants and foods. Both the USDA and the FDA must study the sources of genetically altered plants and foods, and the nature and effects of the transferred genetic material. With this in mind, it might at first seem logical to let one agency take on more of the regulatory responsibility in this area to avoid

redundant regulation. The FDA has essentially left most regulation in the hands of the USDA, as the FDA accepts mere notification that genetically altered foods are entering the market, and does not require even the kind of optional premarket evaluation that was performed for the Flavr-Savr. While this results in important reduced costs for the FDA in the face of budget constraints and limited resources (as manufacturers may expend their own resources by assessing the safety of their own food products prior to marketing), this also results in less stringent FDA regulation. It is uncertain, however, whether a move toward minimal regulation is a wise move to make at such an early stage in the regulation and marketing of genetically altered plant and food products. While the pressures of limited resources and budget constraints are real threats to the FDA's capabilities, the field of biotechnology is too new for relaxed FDA evaluation—especially because the USDA also seems to be following a trend toward more streamlined, more lenient regulation.

As was discussed in Section I, the USDA has already moved away from applying an extensive permit requirement for introducing genetically altered organisms into the environment and toward a more lenient system of notification for six crops. The notification program for field trials of genetically engineered plants may be about to become further streamlined, however. On August 22, 1995, the USDA published a proposed rule in the Federal Register which would further amend 7 CFR §340. The effect of the proposed amendments would be to simplify procedures for the introduction of certain genetically engineered organisms,

requirements for certain determinations of nonregulated status, and procedures for the reporting of field tests conducted under notification. 48 The USDA has articulated several potential amendments to the currently used procedures:

1. Extending Easy Notification. The notification process for introductions of genetically altered products into the environment would be extended to plant types beyond the six plant types now designated for notification in 7 CFR § 340.3. APHIS proposes to allow lenient notification for the field tests of nearly all genetically engineered crops, asserting that there is no technical reason to treat some crop categories differently from others. The only requirements would be that certain eligibility criteria and performance standards are met. Thus, any plant species not listed by the agency as a noxious weed would be allowed to be introduced into the environment.

2. Reduced field test requirements. Instead of requesting annual data reports, APHIS would only require that testing results which are unexpected or adverse are reported to the agency.

~ 60 Fed. Reg. 43567 (August 22, 1995)

~ Remember that the USDA showed its proclivity toward leniency in this area early on by originally proposing to decentralize all decisions to add plant types to the notification list. The proposed amendments to 7 CFR § 340 (57 Fed. Reg. 53036, Nov. 6, 1992) had originally provided for eligibility for plants once consultation with an appropriate Institutional Biosafety committee was conducted. See above discussion of the amendments to 7 CFR §

340.

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(Recordkeeping requirements would remain thorough, as currently provided in 7 CFR §340.).

3. Extending determinations of nonregulated status to plants related to antecedent organisms  
Regulated articles that are closely related to an organism for which a determination of nonregulated status has already been made will easily be able to attain nonregulated status. Thus, as bioengineered plants with similar traits to those already approved for nonregulated status continue to seek USDA approval, the list of nonregulated plants will grow.

4. Publishing guidelines. APHIS will publish general guidelines for field trials of the new products of agricultural biotechnology, including information regarding procedures, methods, scientific principles, and other factors. Any developer may consult APHIS to verify procedures, practices, or protocols to be used.

*Possible Effects of Relaxed Regulation*

Reducing regulatory hurdles for plant introduction seems to conform to the Office of Science and Technology's risk-based approach that is outlined above, as a lenient notification process allows the USDA to focus more on the characteristics and risks posed by finished products than on organism introduction and the methods by which such products are created, which do not in



themselves seem to pose a great degree of risk. However, less stringent permit requirements present a danger of problematic effects—most notably that the number of applications for non-regulated status may significantly increase, and that wholesale deregulation of genetically altered food products may not adequately account for the potential to transfer genes to wild relatives.

One of the effects of the notification procedure is that the cost associated with permit preparation is reduced by 95%.<sup>50</sup> When one considers, however, that the number of existing notifications and introduction permit approvals is already substantial (since 1987, for example, over 560 field test permits have been issued, including 39 different plant species, and APHIS has reviewed and acknowledged over 900 notifications for the 6 originally designated crops), reduced cost associated with USDA notification makes it extremely likely that a sharp upward trend in the number of notifications and introductions of genetically altered organism will be sparked. ~ A notification system enables (and arguably encourages) more widespread biotechnology experimentation, opening up genetic engineering of food to both large and small actors and providing the opportunity for many experiments to be conducted with minimal regulation.<sup>52</sup> Under the proposed rule, it is

~ The industry would save approximately \$50,000 in costs associated with

preparing submissions to APHIS. ~, 60 Fed. Reg. 43567 (August 22, 1995).

51 APHIS recognizes that if its simplified procedures for genetically engineered plants are put into place, there will be growth in experimentation

- but it anticipates only positive effects, such as an increase in agricultural production and a broadening of international trade. The agency also acknowledges that developing researchers would benefit under the new scheme. ~ 60 Fed. Reg. 43567, 43571 (August 22, 1995)

52 I should note that the converse is also problematic. If regulation is .- stringent, the development of genetically engineered products may be crippled.

anticipated that 99% of all field trials would be conducted under notification procedures, and that determinations to grant nonregulated status would take one-fourth of the time now required.

As long as experimentation is conducted responsibly and carefully, this alone does not pose a problem. After all, the goal of regulation is not to stifle research and development—especially in the potentially beneficial, new field of biotechnology. However, a sharp increase in the number of introductions will logically yield an increase in the number of requests to switch from regulated to nonregulated status, as the hundreds of biotechnological research projects currently underway will begin to seek entry into the marketplace for field tested products. It is questionable whether the USDA will have the resources or the experience with genetically altered plants to comfortably accommodate all of these requests. Thus, while the process for assuming non-regulated status is theoretically sufficiently comprehensive to compensate for any leniency in allowing genetically altered products to be introduced through a notification process, the danger exists that the procedure for obtaining non-regulatory status will not be workable in reality.

Two potentially undesirable effects could follow if the USDA is swamped with regulatory requests. Either the agency will be

For example, with extensive review by the USDA for plant and agricultural characteristics, the FDA for food characteristics, and the EPA for insecticidal properties, one could envision a burdensome, expensive process which would be a huge disincentive to companies wishing to develop genetically engineered products. Furthermore, such a process would benefit large, richer companies at the expense of smaller, more entrepreneurial biotech companies. A regulatory position assuming a middle ground is obviously in order.

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clogged with work, or the regulations will become even further lenient. Not only does the USDA not necessarily have the capability or desire to evaluate every product as extensively as it was able to do with the Flavr-Savr, but it also will not be likely to halt the advent of genetically altered agricultural products by scrutinizing each new proposal and causing extensive delay through backlog. One obvious solution to this danger would, then, seem to be the kind of mass USDA approval process for genetically engineered crops that is set forth in the USDA's proposed rule, as me-too kinds of crops may be placed under an extremely simplified review process.

When the USDA instituted its lenient notification process for tomato, cotton, tobacco, corn, potato, and soybean, it emphasized that the USDA's responsibility under the Federal Plant Pest Act and the Plant Quarantine Act is to protect agriculture and the environment against the introduction and dissemination of plant pests, and that this is completely separate from commercialization and marketing concerns, which are left to state laws, the Federal Food, Drug, and Cosmetic Act, and the Federal Insecticide, Fungicide, and Rodenticide Act. The USDA's role is evidently only one in a chain of potential regulation, and should ~ the actions of other entities with discrete responsibilities regarding genetically altered foods, such as the FDA and state authorities.

There are several potential dangers that could result from relaxing the regulations and evaluations of genetically engineered products. The greatest potential danger lies in the possibility (and arguably, probability), that the FDA and individual states

will not elect to institute their own comprehensive evaluative methods for genetically altered products. If this is the situation, and each entity assumes that the other will act when in fact none of them are undertaking strict evaluations, the result may be too many genetically altered foods hitting the market too soon. Every step in introducing genetically altered products into the marketplace (from interstate movement and experimentation to commercialization and marketing), will then be leniently regulated by each organization or entity with a voice in the regulatory process.

Second, just because a plant type is approved for notification does not mean that it carries with it no degree of risk. While the Office of Science and Technology's risk-based evaluation dictates that it is the finished food product that matters, there is a danger that more lenient regulations could result in approval based not even on the ultimate characteristics of the genetically altered food, but on the nature of the traditional, unaltered version of the food (e.g. general approval of all genetically altered tomatoes because normal tomatoes are safe). Through biotechnology, however, one has the ability to radically change the nature of a common food. While products may look alike, after genetic alteration they can have vastly different compositions and manifest their traits very differently. For example, there are a variety of genetically altered tomatoes that have recently been approved or are currently going through regulation; yet, while they all look like tomatoes and taste like tomatoes, they are not all necessarily just like the Flavr-Savr.

DNAP Plant Technology has marketed a tomato with a three ~i~n~h shelf life by isolating the gene that serves as the master switch for ethylene, copying it and reinserting it. Monsanto's genetically altered tomato was developed not only for its extended shelf life, but also to withstand longer travel time. It contains a gene from a soil bacterium used to slow the tomato's production of ethylene. The agencies must keep in mind that there are no predictable bounds to the extent of genetic engineering; every altered product should really be evaluated on its own merit to insure that nontraditional, genetically engineered foods do not have nontraditional effects.

Third, consumers may perceive the existence of genetically altered foods on supermarket shelves as an indication that such foods have been thoroughly tested and approved by regulatory agencies, and thus be more trusting of products that may not in acutality have gone through stringent regulation. It is undoubtedly important to have affirmative agency approval. Early on, industry expressed the need for strong but appropriate oversight by Federal agencies to ensure public confidence in foods produced by. .. new techniques; this was one of the reasons the FDA published its policy statement on foods derived from new plant varieties to begin with. ~ Since genetically altered foods are at the center of public concern in the food industry, consumers may falsely assume that all such foods are being strictly regulated. People have more faith in products that have been authorized by the FDA; for example, initial skepticism regarding the Flayr-Sayr

57 Fed. Reg. 22984 (May 29. 1992)

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largely disappeared once consumers discovered that the FDA had deemed the tomatoes safe for consumption. ~ Furthermore, it would not only be misleading to the public to have only postmarket regulation of genetically altered foods, but public receptivity to such foods could be damaged without affirmative agency approval.

Fourth, mistakes can happen. Any new product or discipline initially requires more comprehensive monitoring; only when a product passes the tests of time can relaxing standards be considered a wise action. Even seemingly common agricultural products that actually do go through extensive regulation can have unanticipated effects. For example, in 1970, 15% of the national corn crop was wiped out by a pathogen because more than three-fourths of the United States' corn acreage was planted with a new hybrid corn seed, and the scientists who derived the seed had not realized that the gene affecting reproduction also influenced susceptibility to fungi. ~ The USDA and the FDA should stringently evaluate genetically altered products until they truly are proven through use and experience.

*A Potential Tool: The Advisability of Labeling*

Imposing labeling requirements has been proposed as a means of avoiding extensive agency involvement in the review process while still providing a way to maintain governmental interest in genetically altered foods through controlling how such products

It's Food, Jim, But Not as We Know It. Suner Marketing, November 4, 1994.

~ 'Promise, Menace of Biotech create Sharp Debate. San Diego Union  
~ Sept. 29, 1994.

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are marketed. This debate has perhaps been most clearly highlighted by the current experience with Bovine Growth Hormone and Bovine Somatotropin in the dairy industry.<sup>56</sup> The issues raised by Bovine Growth Hormone provide a framework from which the labeling of genetically engineered foods in general may be discussed.

Bovine Growth Hormone is a genetically engineered copy of a cow hormone which, when injected into cows, increases their milk production. All milk contains natural BGH; however, when recombinant BGH (rBGH) is injected into cows, traces of it are found in milk. The approval of rBGH in 1994 stirred up a flurry of concerns regarding the regulation of rBGH, the potential for requiring labels on all products which contain rBGH, and the ability of those products which are rBGH-free to have such information on their labels. Vermont was the first state to require the identification of products containing rBGH (it will require signs or shelf stickers for such foods), and it is probable that other states will follow its lead. On the federal level, the USDA and the FDA have both become involved in the debate surrounding rBGH. The USDA has stated that milk from BGH-treated cows is not different than the milk from untreated cows. The FDA published a statement that the FDA has no authority to ban truthful and not misleading statements on labels, thus allowing products to claim they are BGH-free (though not requirin labels).

<sup>56</sup> Bovine Growth Hormone and Bovine Somatotropin are essentially the same substances. Both can be produced through the use of recombinant techniques and are abbreviated as rBGH and rBST, respectively.

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Those who support labeling cite several reasons for their stance— many of which parallel objections made regarding the general existence and use of genetically altered foods (see Section I)— but anxiety generally stems from fear of the effects of ingesting synthetic matter on a regular basis. Through the use of rBGH, humans ingest higher than normal levels of BGH. Also, rBGH injections have caused health problems in cows. Furthermore, some argue that the public has a right to know which products are genetically altered, and that such information should not be hidden from them.

The FDA, however, has not embraced the idea of labeling genetically engineered foods, as the agency has not found characteristics of genetically engineered foods to universally differ from foods developed by other breeding methods to the extent that labeling would be necessary.<sup>57</sup> The FDA policy on labeling, which was explained in the FDA's 1992 policy statement on genetically altered foods, requires labeling only if a food derived from a new plant variety differs from its traditional counterpart such that the common or usual name no longer applies to the new food, or if a safety or usage issue exists to which consumers must be alerted. Products using traditional plant breeding techniques are not subject to labeling requirements despite being modified with techniques such as hybridization and

<sup>57</sup>The United States is not the only country with labeling concerns. In Europe, the European Union ministers agreed to rules for marketing and labeling genetically engineered foods, requiring labeling only when a product differs from its natural counterpart, and not requiring comprehensive labeling. For example, a tomato with a protein from another fruit or vegetable would need a label, while sugar produced from a beet that had been genetically modified to resist disease would not have to be labeled.



mutagenesis (for example, there are many genetically distinct tomatoes in the United States derived from natural breeding techniques— they do not require specific labels simply because they have different traits); it is not clear that foods modified through biotechnology should be subject to a different rule. The FDA policy does require some labels, but only when they are necessary to alert the consumer to a safety issue or to a difference in a food from its traditional variety, such as when a gene from a food that could cause an allergic reaction is transferred into another food, or when a food's composition is changed significantly (e.g. taking the vitamin C out of an orange). Presumably, agency oversight of genetically altered products is adequate to detect these narrow kinds of safety issues.

There are other reasons to discourage mandatory labeling of genetically altered foods. Henry Miller, who was an official in the FDA from 1979 to 1994, recently stated that even a strictly accurate message can mislead and confuse consumers if it is irrelevant, unintelligible, or tells only part of the truth. Consumers only need labels that give them information about a product's safety. 58 In addition, labels that are cluttered with too much information about the product may be ineffective by deemphasizing the most important nutritional qualities of a product. Furthermore, it is unclear how many steps removed from a genetically engineered product a food would have to be before a label would no longer be required. As Miller stated in the

<sup>58</sup>Henry Miller, A Label We Don't Need, Wall Street Journal, March 18, 1996, at A18.

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abovementioned article: Would special labels be required for pizza or burritos containing cheese made with new-biotech-produced chymosin (renin)? Or for chickens raised on feed from new biotech-manipulated corn, or vaccinated with a new biotech vaccine?. In addition, imposing universal labeling requirements for genetically altered foods would add to such foods' production costs— Miller anticipated having to segregate all biotech foods through planting, harvesting, processing, ~ distribution— and would competitively disadvantage genetically altered products in the marketplace.

Finally, if labels were to be required prematurely at this new stage in the development and marketing of genetically altered products, foods labeled as being genetically engineered may be irrationally avoided among consumers. Rigid labeling requirements are not likely to do anything but cause consumers to discriminate against genetically engineered foods. As has been the experience with nutrition labeling in general, labels are ineffective without a basic education as to what the information on the labels means in a practical sense. Until the USDA and the FDA can impart to consumers trustworthy, tested information about genetically engineered products, the public will remain skeptical, and perceptions that genetically altered foods are potentially threatening and unnatural will persist. The experience with rBGH/rBST in Vermont is a case in point. A group named Food & Water has aroused fears over rBGH, turning the public against the substance and demanding that labels indicate products which are rBGH-free. Merely providing a label at this point would

exacerbate the public's anxiety and steer the public away from certain products. Perhaps the controversy in Vermont could have been alleviated with educating the public instead of letting the people get swept up with potentially groundless fears.

The key is not to blindly label all genetically altered food products. Instead, it is to educate the public in the field of genetic manipulation— a highly technical field now dominated by experts— and to welcome lay participation in designing a scheme for the regulation of genetically engineered foods. While food producers have a right to advertise that they do ~ use genetic engineering techniques, even this information may eventually be recognized as superfluous by the educated consumer.

#### *A Possibility for Reaulatorv CooDeration*

The FDA and the USDA both need to maintain relatively comprehensive analyses of genetically altered products because each agency ultimately focuses on different issues in its respective sphere. Although the USDA and the FDA ostensibly both focus on the safety of the plant and the nature of the transferred genetic material, the bulk of the USDA's inquiries relate to agricultural effects, while the FDA is concerned with effects on food and humans. For example, the kinds of plant pest characteristics that the USDA considers relate to the susceptibility of the plant to disease, and its impact on other plants and organisms. In contrast, the FDA focuses on effects on food products such as toxicity, nutrient content, allergens, and antibiotic resistance. While both of these areas are crucial

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inquiries, they do not completely overlap. It is possible, therefore, that if the USDA was to be the only agency to give premarket regulatory approval to genetically altered products (thus giving biotechnology manufacturers license to enter genetically altered foods into the United States markets), and the FDA was only to impose postmarket controls, that an essential, distinct area of analysis could potentially be overlooked (or at least only spot checked). It is uncertain whether industry recommendations for the development of new genetically altered foods, potential labeling requirements, and postmarket controls are enough to insure that the quality of such food products will be sufficiently monitored, given public hesitancy toward biotechnology and the fact that most of the genetically altered products have not yet been widely tested on the market.

There is, however, a possibility for the kind of regulatory cooperation that was endorsed in the Coordinated Framework. Interestingly, the differing natures of the USDA and FDA inquiries correspond to the distinction between agronomic and quality characteristics that the FDA described in its 1992 policy statement. Since both agronomic and quality characteristics can be evaluated through similar data, perhaps a viable system could be set up whereby obtaining non-regulated status could be accomplished through a dual agronomic/quality analysis of the genetically altered product. Manufacturers could be responsible for submitting one set of information (including identity information, experiment results, pertinent scientific and general publications, etc.), and the USDA and the FDA could then evaluate

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this information separately for agronomic and quality characteristics. When the USDA decides that an article is agronomically safe, that product could in turn be evaluated by the FDA for quality control, even utilizing the USDA's results as an analytical tool for expediency.

Even though this scheme would impose a great deal of regulatory responsibility upon the FDA that it is not necessarily statutorily obligated to take on, it would be advisable for a system such as this one to remain in place for at least a few years— a process which could gradually be streamlined as the agencies, the market, and the public have sufficient experience with genetically altered foods. ~ Food additives have been deemed important enough for Congress to mandate premarket approval; genetically altered products may present similar concerns about safety, as new materials are added to traditional plant and food varieties. Especially because genetically engineered products are rapidly becoming more complex, the FDA should have an interest in premarket evaluation. (Virus-resistant squash, for example, is likely to be much more complicated than the Flavr-Savr tomato.) At least until the FDA has sufficient experience with enough finished genetically altered whole foods to decide that genetic

~ A sign that the American people are not satisfied with the degree of federal regulation of genetically altered foods is Minnesota's state rules regulating genetically engineered organisms used in agricultural production or processing. The state legislation has a system of release permits and notification, with commercial exemptions for materials which have gone through federal agency approval procedures (the Flavr-Savr earned such an exemption) Arguably, if federal level regulation was deemed sufficient, such a state procedure would not need to exist. Additionally, regulation would ideally be at the federal and not at the state level, as agricultural products and foods have the potential to have widespread adverse impacts despite isolated state regulations.

engineering processes present no significant element of danger and that the public has a sufficient base of knowledge regarding genetically altered foods (e.g. that the public is not exposed to allergens, toxins, or products with diminished nutritional value, that the environment is not adversely affected, and that consumers are comfortable with the products), premarket regulatory evaluation is in the public interest. As different technologies are tested, approved, and marketed, the process of evaluation may naturally become easier. At such a point, less resource intensive methods could potentially come into play. However, only when the time is right to increase regulatory leniency over genetically altered foods should such methods be emphasized.

#### Conclusion

The key to knowledge is information; the key to information is research. The USDA and the FDA should not cut corners before genetically altered plants and food products are sufficiently established in the marketplace. Through cooperation, each agency can efficiently assess essential information and insure that the genetically altered products that enter the United States markets are reliable. Continuous dialogue not only between agencies, but also between the regulatory and the private sectors is crucial to establish a rational response to the new technology. There is evidence of a current trend towards a more heightened sense of agency awareness in this field. For example, the FDA recently announced the scheduling of a comprehensive discussion of the scientific criteria and principles generally agreed upon by

scientists in the food safety community as necessary for demonstrating that a food ingredient is safe. 60 This discussion, which will occur on May 15, 1996, will be open to the public, and will address the fact that the advent of new technologies such as genetic engineering of traditional foods and novel uses of plant products. .. present new situations for which an alternative approach to safety assessment may be needed. 61 Such initiative by an agency to ascertain the need for information on the safety of genetically engineered plants and foods is a welcome step, given the popular demand for governmental and scientific response to the development of such products. After all, even if the introduction of products altered by biotechnology is not (and should not be) considered by the agencies quite as an attack of killer foods that requires all out national retaliation, at the very least, it should be considered a substantial enough incident to merit a material level of police action.

60 61 Fed. Reg. 8291 (March 4, 1996)

61 61 Fed. Reg. 8291 (March 4, 1996)

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